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Running title: Desert dust and health outcomes in Southern Europe

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Abstract

Background: Evidence on the association between short-term exposure to desert dust and health outcomes is controversial.

Objectives: To estimate the short-term effects of particulate matter $\leq 10 \mu\text{m}$ (PM_{10}) on mortality and hospital admissions in 13 south-European cities, distinguishing between PM_{10} originating from desert and from other sources.

Methods: We identified desert dust advection days in multiple Mediterranean areas for 2001-2010 by combining modelling tools, back-trajectories and satellite data. For each advection day, we estimated PM_{10} concentrations originating from desert, and computed PM_{10} from other sources by difference. We fitted city-specific Poisson regression models to estimate the association between PM from different sources (desert and non-desert) and daily mortality and emergency hospitalizations. Finally, we pooled city-specific results in a random-effects meta-analysis.

Results: On average, 15% of days were impacted by desert dust at ground level (desert $\text{PM}_{10} > 0 \mu\text{g}/\text{m}^3$). Most episodes occurred in spring-summer, with increasing gradient of both frequency and intensity North-South and West-East of the Mediterranean basin. We found significant associations of both PM_{10} concentrations with mortality. Increases of $10\text{-}\mu\text{g}/\text{m}^3$ in non-desert and desert PM_{10} (lag 0-1 days) were associated with increases in natural mortality of 0.55% (95% CI: 0.24, 0.87%) and 0.65% (95% CI: 0.24, 1.06%), respectively. Similar associations were estimated for cardio-respiratory mortality and hospital admissions.

Conclusions: PM_{10} originated from desert was positively associated with mortality and hospitalizations in Southern Europe. Policy measures should aim at reducing population

exposure to anthropogenic airborne particles even in areas with large contribution from desert dust advections.

Introduction

The International Panel on Climate Change (IPCC) has estimated that most of the atmospheric particles worldwide are emitted by natural sources, with mineral dust from arid regions being the second after marine aerosol (IPCC 2007). The main source areas of dust particles are located in the arid regions of the planet, and Sahara and the Arabian Peninsula have been identified as the major contributors over the globe (Prospero et al. 2002). The Mediterranean basin is especially vulnerable to injections of desert dust because of its proximity to Sahara to the south and to the Arabian Peninsula to the east. Over the Mediterranean, desert dust outbreaks are caused by certain meteorological scenarios, well characterized for both western, central and eastern sides of the basin (Escudero et al. 2005; Gkikas et al. 2013; Kalivitis et al. 2007; Querol et al. 2009b; Salvador et al. 2014).

Short-term effects of particulate matter (PM) have been widely documented in the epidemiological literature (Pope and Dockery 2006). The fine fraction of PM (generally identified in the size range < 2.5 micron – $PM_{2.5}$) has long been considered the one mostly responsible for the adverse health effects, because it can easily reach the lower respiratory system and influence the circulatory system (Pope and Dockery 2006). Most of the research is now focusing on the major components and sources of PM, including organic constituents and metals originating from traffic emissions and other combustion processes. However, a debate on the potential health effects of coarse particles (PM in the range 2.5-10 microns, $PM_{2.5-10}$) has been stimulated by a systematic review from Brunekreef and Forsberg (2005), where the authors concluded that coarse and fine PM exert similar effects on respiratory outcomes, and supported the plausibility of an association between $PM_{2.5-10}$ and cardiovascular outcomes. Among the major constituents of coarse PM, crustal materials, re-suspended dust, sea salts, desert dust, and

biogenic components have been identified (Perrino et al. 2009; Pope and Dockery 2006; Querol et al. 2009b). However, doubt remains on the relative toxicity of these components and, in particular, on whether natural sources of PM represent a threat to human health. Several studies have been conducted in the last few years in single cities of Southern Europe, all evaluating whether the short-term association between PM and mortality/hospitalizations would be enhanced on days characterized by desert dust advections, with inconsistent results (Karanasiou et al. 2012).

We have previously shown results of the associations between short-term exposure to both fine and coarse particles with mortality (Samoli et al. 2013, 2014) and hospital admissions (Stafoggia et al. 2013) in multiple cities of South Europe. The aim of the present study is to describe the geographic distribution of PM₁₀ concentrations from desert dust and other sources in the Euro-Mediterranean area, and report estimates of their short-term effects on mortality and emergency hospitalizations. The work was conducted within the EU-funded project “Particles size and composition in Mediterranean countries: geographical variability and short term health effects” (MED-PARTICLES 2010).

Methods

Setting

The study was conducted for the period 2001-2010 in 13 European cities of the Mediterranean basin: Barcelona and Madrid (Spain), Marseille (France), Bologna, Milan, Modena, Palermo, Parma, Reggio-Emilia, Rome and Turin (Italy), Athens and Thessaloniki (Greece). Modena, Parma and Reggio Emilia have been analyzed altogether as a single conurbation called “Emilia Romagna” since they are very close and share common environmental and socio-demographic

characteristics. The Mediterranean area is characterized by specific characteristics, such as highly urbanized areas in which traffic congestion occurs regularly, elevated sea traffic due to tourism and shipping activities over the Mediterranean Sea, and enhanced formation and accumulation of atmospheric pollutants as a result of diverse meteorological and topographical causes (Querol et al. 2009a). In addition, the entire area is frequently affected by outflows from North African deserts, especially from February to October, but with different seasonal incidences western to eastern across the region (Pey et al. 2013).

Health data

For each city, we collected information on daily counts of death from natural (International Classification of Diseases, 9th or 10th revisions – ICD9/ICD10 codes: 1-799/A00-R99), cardiovascular (ICD9/ICD10 codes: 390-459/I00-I99) and respiratory causes (ICD9/ICD10 codes: 460-519/J00-J99). Similarly, we retrieved information on hospital emergency admissions from the hospital discharge databases of each country, as previously described (Stafoggia et al. 2013). For each hospitalization we collected information on the primary diagnosis and the age of the patient, and considered three study outcomes defined on the same ICD codes as those used for mortality: cardiovascular and respiratory admissions for patients 15+ years old, respiratory admissions in the age group 0-14 years. Since data were anonymous and collected as daily counts, no informed consent was needed, and the study was exempted from formal institutional review.

Exposures

Daily concentrations of PM₁₀, PM_{2.5} and PM_{2.5-10} were retrieved in each city of the study from the regional Environmental Protection Agencies (EPAs). Further details are reported in Stafoggia

et al. (2013). Urban background monitoring stations were given priority because they better represent average exposure of the population. When they were missing, they were replaced with traffic monitor, as long as the station was not directly influenced by proximal major roads. When data from multiple monitors were available, they were averaged and missing data were imputed using standard procedures, as described in Samoli et al. (2013) and Stafoggia et al. (2013).

Desert dust advection days were identified in each study area using a combination of tools, including meteorological products (NCEP/NCAR), aerosol maps (BSC-DREAM; NAAPS-NRL; SKIRON), air masses back-trajectories (HYSPLIT), and satellite images (Sea-WiFS). Further details are reported in Pey et al. (2013). Once dust outbreaks were detected in each study area, African dust contributions were quantified for every single day in the outbreak by applying the reference European Union (EU) method (Escudero et al. 2007). This validated procedure computes the expected PM_{10} concentrations at rural monitoring sites in absence of African dust advection by using 30-day moving 40th percentile to the PM_{10} data series not containing those days impacted by African dust. This results in the estimated background PM, while the Saharan dust contribution (desert PM) is estimated as the difference between the observed PM_{10} and the estimated background PM (Escudero et al. 2007; Pey et al. 2013). Daily PM_{10} concentrations from desert dust within the city were attributed from the closest rural background site, as described above, under the assumption that the contribution in the city would be the same as that estimated at the rural site, given the wide spatial distribution of African dust advections. Finally, we computed the amount of daily PM_{10} concentrations due to other sources (non-desert PM_{10}) by subtracting the desert PM_{10} component from the total concentrations. Unfortunately, the same approach could not be applied on $PM_{2.5}$ and $PM_{2.5-10}$ due to the lack of $PM_{2.5}$ rural monitoring

network operating daily for multiple years in all locations. Therefore, daily concentrations of fine and coarse PM were only used for descriptive purposes.

Other data

Other environmental and time trend variables were collected. They include: daily ozone concentrations (from EPAs), air temperature (from the closest airport if available, or city monitors otherwise), influenza epidemics (estimated from National surveillance systems if available or an index based on respiratory mortality, otherwise based on daily counts of influenza admissions), public holidays (a two-level variable identifying national holidays) and summer population decrease (a three-level variable assuming value 2 in the two-week period around mid-August, value 1 from mid-July to end of August, with the exception of the aforementioned two-week period, and value 0 otherwise). See Samoli et al. (2013) and Stafoggia et al. (2013) for additional details.

Statistical analysis

The analyses were carried out in two stages, with city-specific analysis in the first stage followed by random-effects multivariate meta-analysis.

In each city, we fitted over-dispersed Poisson regression models, where the daily counts of cause-specific mortality/hospitalization were related with daily mean PM₁₀ concentrations while adjusting for potential confounders. The list of confounding variables was chosen a priori and was the same in each city. It included: time trends, air temperature, public holidays, summer population decrease, and influenza epidemics. Long-term and seasonal time trends were adjusted for by introducing a three-way interaction term between year, month, and day of the week. This method has been demonstrated to be equivalent to a case-crossover design using a “time-

stratified” approach to select control days (Levy et al. 2001; Lu and Zeger 2007; Maclure 1991). We adjusted for temperature by using separate natural splines for high temperatures (lag 0-1) and low temperatures (lag 1-6), as described before (Stafoggia et al. 2013). This method is very flexible in capturing potential delayed and nonlinear effects of high and low temperatures on health endpoints, an issue very relevant in the present study due to the strong seasonality of health outcomes, PM exposures and dust advections. We did not adjust for humidity or other meteorological parameters because the evidence on their short-term health effects is weak and inconsistent (Katsouyanni et al. 2009). Finally, public holidays, summer population decreases and influenza epidemics were modeled using indicator variables.

Once the adjustment model was defined, we added the exposure term(s). Associations between the study outcomes and total PM₁₀ were estimated using single-pollutant models. In addition, we used two-pollutant models that included both desert and non-desert PM₁₀ concentrations to estimate independent associations with source-specific PM₁₀ exposures. The lag structure between PM₁₀ and mortality/hospitalization was chosen a priori based on previous results in the same cities (Samoli et al. 2013; Stafoggia et al. 2013): the average exposure of the current and previous day (lag 0-1) was used in relation to natural mortality and cardiovascular admissions, while the average of the last six days exposure (lag 0-5) was used for cardio-respiratory mortality and respiratory hospital admissions.

Additional analyses were performed. First, we evaluated effect modification by season, defined as cold (October to March) and warm (April to September). This analysis was motivated by previous results showing higher associations between PM exposures and health outcomes in the warmer months, and by desert dust advections having a strong seasonality in terms of both

occurrence and intensity of the episodes, with different patterns western to eastern along the Mediterranean basin (Pey et al. 2013). Effect modification was assessed by stratifying the source-specific PM models by season. Second, we investigated the concentration-response functions between desert and non-desert PM₁₀ and natural mortality by fitting, for each city, a natural spline model for the exposures with two equally-spaced inner knots, and pooling the city-specific estimates using a meta-smoothing approach (Schwartz and Zanobetti 2000). As a final check, we evaluated whether the estimated main effect of PM₁₀ was modified during desert dust days using an interaction term between the desert dust indicator (yes/no) and total PM₁₀ concentration.

Third, we tested whether desert dust days were associated with increased mortality and hospitalizations as an independent risk factor, by adding a dichotomous exposure variable (desert dust yes/no) in the regression model.

Finally, we evaluated desert days as an effect modifier of the PM₁₀-mortality association using an interaction term.

In the second stage of the analysis, we pooled the city-specific results using random-effects multivariate meta-analytical procedures according to the method proposed by Jackson et al. (2010), in order to account for within-city covariance of effect estimates from the two-pollutant models. We tested heterogeneity among the city-specific results by applying the X^2 test from Cochran's Q statistic, and estimated the amount of heterogeneity by computing the I^2 statistic (Higgins and Thompson 2002), which represents the proportion of total variation in effect estimates due to between-cities heterogeneity. All results are expressed as percent increases in mortality/hospitalizations, with 95% confidence intervals (CI), relative to 10 $\mu\text{g}/\text{m}^3$ increments in

the pollutants. All first-stage analyses were fit using R, version 3.0.2 (R development Core Team (2011), URL <http://R-project.org>). Meta-analyses were conducted using Stata, version 11 (StataCorp, College Station, TX, USA).

Results

Exposures

The annual frequency of dust advection days with dust impacting at ground level (desert PM₁₀ > 0 µg/m³) was 15% across the study areas and ranged between 28.5% in Palermo and 8.8% in Emilia-Romagna, with a clear increasing trend from North to South and towards the centre of the Mediterranean basin (Table 1). We found differences in the seasonality of Saharan dust outbreaks across locations, with summer-spring peaks in the western cities and similar frequencies in colder and warmer months in Greece (Supplemental Material, Figure S1). During desert dust days, mean total PM₁₀ concentrations ranged from 54 µg/m³ in Athens and Thessaloniki to 33.1 µg/m³ in Marseille, with desert PM₁₀ concentrations amounting to 25 to 40% of the total PM₁₀ (Supplemental Material, Table S1). In general, coarse PM concentrations were higher in southern cities during dust days, while no clear geographical pattern is discernible with regard to fine PM. In addition, total PM₁₀ concentrations were usually higher on desert dust days than on other days, with a more pronounced difference in southern cities compared with northern cities. City-specific correlations between the environmental variables are reported in the Supplemental Material, Table S2. Table 2 displays the estimated differences between desert dust advection days and no-dust days in terms of daily mean PM, ozone and air temperature, based on a multivariate linear regression model adjusted for month. Both city-specific and pooled results are reported. Once seasonality was taken into account, we found a sharp increase in PM during dust days, with PM₁₀ variations ranging from 8.8 µg/m³ in Rome to 21.7 µg/m³ in Athens. The

greatest differences between dust days and other days were found for fine particles in Madrid and Barcelona, while coarse particles seemed to be more affected by dust advection in Madrid and Athens. Overall, predicted particulate concentrations increased by 13.4 ± 1.5 , 6.9 ± 0.9 and $6.2 \pm 1.4 \mu\text{g}/\text{m}^3$ on dust days for total PM_{10} , $\text{PM}_{2.5}$ and $\text{PM}_{2.5-10}$, respectively. Ozone concentrations were similar during desert dust advections and other days (estimated mean difference $-1.8 \pm 1.8 \mu\text{g}/\text{m}^3$) but air temperature was $2.2 \pm 0.2^\circ\text{C}$ higher on dust days after seasonality adjustment (Table 2).

Association of exposures with mortality/hospitalizations

The mean daily counts of total natural mortality ranged from 11 in Bologna to 81 in Athens, and mean numbers of combined cardiovascular and respiratory admissions among those ≥ 15 years of age ranged from 24 in Palermo to 189 in Madrid (Supplemental Material, Table S3). Three cities (Marseille, Athens and Thessaloniki) contributed only to the mortality analysis. All cities contributed with at least three complete years of daily observations.

Table 3 shows the associations between total PM_{10} (from single-pollutant models) and source-specific PM_{10} (from two-pollutant models) with daily mortality and hospital admissions. Total PM_{10} was associated with all the study outcomes: increments of $10 \mu\text{g}/\text{m}^3$ were associated with 0.51% (lag 0-1, 95% CI: 0.27, 0.75%), 0.66% (lag 0-5, 95% CI: -0.02, 1.34%) and 2.01% (lag 0-5, 95% CI: 0.92, 3.12%) increases in natural, cardiovascular and respiratory mortality, respectively. Similar results were found for cardio-respiratory admissions. Associations of mortality and hospitalizations with $10 \mu\text{g}/\text{m}^3$ increases of desert and non-desert PM_{10} were similar for all natural mortality (0.65%; 95% CI: 0.24, 1.06 and 0.55%; 95% CI: 0.24, 0.87, respectively), though the association with desert dust appeared stronger for cardiovascular

mortality (1.10%; 95% CI: 0.16, 2.06 compared with 0.49%; 95% CI: -0.31, 1.29 for non-desert dust) and weaker for respiratory mortality (1.28%; 95% CI: -0.42, 3.01 compared with 2.46%; 95% CI: 0.96, 3.98). In general, city-specific estimates of the association with desert PM₁₀ were homogeneous (p-value of heterogeneity > 0.05), while consistent heterogeneity was found for the association of non-desert PM₁₀ with cardio-respiratory mortality and cardiovascular admissions (p-value < 0.05) (Table 3 and Figure 1). Within-city differences between associations of natural mortality with desert and non-desert PM₁₀ were not significant (pooled p-value 0.72) except in Barcelona where the association was stronger for non-desert PM₁₀ (1.36%; 95% CI: 0.70, 2.03) than desert PM₁₀ (-0.16%; 95% CI: -1.57, 1.27) (p = 0.05).

We tested whether desert dust days were associated with increased mortality and hospitalizations as an independent risk factor. When a dichotomous exposure variable (desert dust yes/no) was evaluated, we found a weak evidence of dust being a risk factor per se, with % increases of mortality on dust versus no-dust days equal to 0.94% (95% CI: 0.07, 1.81%), 0.67% (95% CI: -2.38, 3.82%) and 0.21% (95% CI: -3.50, 4.06%) for natural, cardiovascular and respiratory causes, respectively. Estimates for admissions were 0.47% (95% CI: -0.50, 1.46%), 0.85% (95% CI: -0.75, 2.47%) and 2.66% (95% CI: -0.19, 5.59%) for cardiovascular (age 15+), respiratory (age 15+) and respiratory (age 0-14) diseases, respectively (data not shown). We also evaluated desert days as an effect modifier of the PM₁₀-mortality association using an interaction term. We obtained similar associations between total PM₁₀ and natural mortality on dust and no-dust days, with estimates, per 10 µg/m³, respectively of 0.74% (95% CI: 0.25, 1.23%) and 0.48% (95% CI: 0.18, 0.78%). A similar result was obtained when we evaluated dust advection as an effect modifier of the non-desert PM₁₀ – mortality association (data not shown).

Results of the effect modification by season are reported in Figure 2. As expected, associations with $10 \mu\text{g}/\text{m}^3$ increases in both PM_{10} sources were stronger during the warmer season.

However, associations with PM_{10} during the spring and summer months were always stronger for non-desert PM_{10} than desert PM_{10} . Associations with respiratory admissions during warmer months were the strongest for both exposures, but also were imprecise (12.4%; 95% CI: 6.00, 19.18% and 5.51%; 95% CI: -1.29, 12.78% for $10 \mu\text{g}/\text{m}^3$ increases in non-desert and desert PM_{10} , respectively).

Finally, the pooled concentration-response functions between non-desert and desert PM_{10} with natural mortality are displayed in Figure S2 of the Supplemental Material. We found increasing risks of mortality for non-desert PM_{10} concentrations rising up to $60 \mu\text{g}/\text{m}^3$, with a flattening of the relationship for higher values of PM_{10} . In contrast, the relationship with desert PM_{10} was linear, though the estimates at higher concentrations were affected by large statistical uncertainty. For each city, we have compared the spline and the linear model with likelihood-ratio tests: most of the cities were consistent with a linear association between natural mortality and desert PM_{10} , and a few of them were consistent with a non-linear relationship with non-desert PM_{10} (Table S4 of the Supplemental Material).

Discussion

To our knowledge, this is the first study investigating the association between PM_{10} originating from desert and non-desert sources with health outcomes in multiple European locations of the Mediterranean area. We estimated statistically significant associations of both PM_{10} sources with mortality and hospital admissions, with no major differences in the magnitude of effects both overall and within cities. Several studies have been conducted in the last years in Southern

Europe evaluating the possible role of desert dust advection as effect modifier in the relationship between PM exposure and mortality. The first study from Perez and colleagues (2008) reported higher association of the coarse PM with natural mortality on dust days than no-dust days in Barcelona, while no differences were found for fine PM (Perez et al. 2008). A few years later the same authors evaluated cause-specific mortality, finding evidence of an effect modification induced by dust advection on cardiovascular mortality only (Perez et al. 2012b), thus confirming the results previously reported in Rome (Mallone et al. 2011) and Madrid (Tobias et al. 2011), and later replicated in Nicosia, Cyprus (Neophytou et al. 2013). On the other hand, two studies conducted in Athens (Samoli et al. 2011a) and Emilia Romagna (Zauli Sajani et al. 2011) showed desert dust outbreaks as being an independent risk factor for mortality, but they questioned its potential role as modifier of the PM-mortality association because they estimated similar associations in dust and no-dust days (Zauli-Sajani et al. 2011) or statistically significant associations with PM on no-dust days only (Samoli et al. 2011a). The same inconsistencies emerge from the few studies conducted in Southern Europe on morbidity endpoints (Alessandrini et al. 2013; Middleton et al. 2008; Reyes et al. 2014; Samoli et al. 2011b).

The present study was designed to compare the associations of the sources of PM₁₀, desert and non-desert, with mortality and hospitalizations. On this regard, it is not directly comparable with the aforementioned studies because size-specific PM associations were not reported and the effect modification was only marginally investigated as a secondary analysis, whereas in the primary approach, two-exposure models with no interaction terms, no formal effect modification hypothesis was tested. Nonetheless, we reached the same conclusion that desert dust advections represent a threat for human health, and that the health effects of dust-derived PM₁₀ are of the same (or similar) magnitude as those reported for anthropogenic sources of air pollution.

Specifically, we also compared the estimates of association between non-desert and desert PM₁₀ with natural mortality in each city and overall, and found no evidence of heterogeneity in the two estimates in most of the cities. The only other study which applied a similar design was conducted in Barcelona (Perez et al. 2012a), and reported stronger associations with PM₁₀ during dust days as compared to no-dust days, especially for the fraction of PM₁₀ not originated from desert sources. It should be noted that when we applied the effect modification analysis on either total PM₁₀ or non-desert PM₁₀ with a desert dust indicator (yes/no), we obtained similar results as those found in other studies: similar associations with PM₁₀ on dust and no-dust days.

The plausibility of health effects due to desert PM exposure is supported by several studies. Numerous species of fungi, bacteria and viruses have been found on many dust samples, and authors speculated that the transport of microorganisms, especially over water bodies, would be favored by the tolerable humidity levels and attenuation of UV by the particle load of dust clouds (Griffin 2007). Furthermore, the toxicity of desert dust might be enhanced by the mixing with anthropogenic sources of air pollution during cloud formation or capture in downwind transport (adsorption of pesticides, industrial emissions, etc.) (Rodriguez et al. 2001). Similarly, specific desert dust episodes are associated with a lowering of the mixing layer height, thus enhancing local and regional atmospheric pollution (and increasing fine as well as coarse PM) from all sources and consequently increasing mortality. Such hypothesis has been recently confirmed over Barcelona by Pandolfi et al. (2014).

Different source areas and patterns of transport to western and eastern Mediterranean could also be responsible for different toxicological properties of desert dust, and therefore partially explain the inconsistencies in previous epidemiological results. Though the Arabian Peninsula is a large

source of atmospheric dust overall, such particles have an influence only in the extreme East of the Mediterranean. Our previous article on dust exposure (Pey et al. 2013) revealed an impact from this region only in Cyprus but not westwards. Therefore, we have assumed that all the cities included in this study were only impacted by Saharan dust advection episodes. Middleton and Goudie (2001) identified South Algeria and West Sahara as the major source areas for dust transport in the Western Mediterranean basin. In contrast, Eastern Mediterranean would be more affected by dust transported by air masses from Libya and Egypt (Kallos et al. 2006). The different regions of the Sahara desert have been shown to have distinct mineralogical properties (Moreno et al. 2006), likely affecting their toxicological potential. Also, dust transport over western and eastern sides of the Mediterranean is characterized by different mechanisms. African dust episodes over the western and central basin are very frequent in spring-summer, although moderate in intensity due to the intricate transport processes (dust travels at very high altitudes) (Karanasiou et al. 2012). In contrast, desert dust transport in the eastern basin is typically induced by cyclones moving eastwards across the Mediterranean and North Africa, transporting dust at surface levels (Pey et al. 2013). These flows may be enhanced under specific scenarios (Moulin et al. 1998) giving rise to short but intense dust episodes.

Associations with desert and non-desert PM₁₀ were stronger during the warmer months. This has been already reported (Samoli et al. 2013; Stafoggia et al. 2013). We also found slightly weaker associations with desert PM₁₀ than non-desert PM₁₀ during the warmer season. This could have had an impact on the overall estimates due to the higher frequency of dust outbreaks in spring and summer. However, it is possible that higher air conditioning use during desert dust days could have reduced effects estimates for desert PM₁₀. A limitation of our approach has been to classify season in two broad six-month time windows, while we have shown dust occurrence

being different in spring and summer months. However, it was not possible to use a finer classification of season in the epidemiological analysis of effect modification due to power constraints.

The main strength of the study has been the application of a standardized protocol for desert dust detection and quantification, coupled with health data collection and epidemiological investigation in multiple cities of the Euro-Mediterranean area. Advanced modelling outputs and satellite images have been applied on a large spatio-temporal scale covering four countries and 10 years of daily observations. Secondly, we were able to separate different sources of particulate matter by applying official EU methodologies, and could disentangle the independent short-term health effects of desert and non-desert PM₁₀. Thirdly, we evaluated both mortality and hospital admissions as study outcomes, thus providing valuable information on the potential mechanisms underlying the reported health effects. Major limitations include the lack of experimental measurements of mineral dust during desert dust advections, and the lack of PM speciation data characterizing the composition of particulate matter during dust and no-dust days. Furthermore, we were unable to quantify the desert contribution to daily fine and coarse PM concentrations due to the few data available on PM_{2.5} and PM_{2.5-10} at rural background monitoring sites. It should be noted that our statistics on desert dust days are not equal to previous reports (Pey et al. 2013; Querol et al. 2009b) as we considered a desert dust day when both desert advection was identified through operational models and desert PM₁₀ estimated concentration was more than 0 µg/m³. Finally, we have used PM concentrations from fixed ambient monitors to infer individual exposures: this might have induced exposure misclassification with Berkson-type error, with possible loss of precision but no induced bias on the regression estimates.

Conclusions

Our results provide consistent evidence that desert dust outbreaks are an important risk factor to human health, and that exposure to PM originated by such natural events is not harmless. In particular, we estimated excess mortality and hospitalizations associated to desert PM₁₀ of the same magnitude as those reported for non-desert PM₁₀.

One of the consequences of climate change is the acceleration of desertification processes in arid and semi-arid regions, which implies an increase in dust outbreaks in the near future (IPCC 2007). Evidence of adverse health effects of both desert and non-desert sources strengthens the need to control for anthropogenic sources, especially on days when desert dust levels are high.. Therefore, steps should be undertaken at local and regional level to ensure public health protection, by reducing anthropogenic emissions and population exposure especially on desert dust advection days.

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Table 1. Occurrence of desert dust days in the eleven cities of the MED-PARTICLES project [n (%)]

City ^a	Study period	Days without desert dust ^b	Days with desert dust ^b	Total days
Milan	2007-2010	1,277 (87.4)	171 (11.7)	1,461 (100.0)
Turin	2006-2010	1,612 (88.3)	199 (10.9)	1,826 (100.0)
Emilia-Romagna ^c	2008-2010	988 (90.1)	96 (8.8)	1,096 (100.0)
Bologna	2006-2010	1,578 (86.4)	203 (11.1)	1,826 (100.0)
Marseille	2006-2008	882 (80.5)	195 (17.8)	1,096 (100.0)
Rome	2005-2010	1,809 (82.6)	360 (16.4)	2,191 (100.0)
Barcelona	2003-2010	2,518 (86.2)	365 (12.5)	2,922 (100.0)
Thessaloniki	2007-2009	898 (81.9)	110 (10.0)	1,096 (100.0)
Madrid	2001-2009	2,714 (82.6)	446 (13.6)	3,287 (100.0)
Palermo	2006-2009	976 (66.8)	417 (28.5)	1,462 (100.0)
Athens	2007-2009	775 (70.7)	282 (25.7)	1,096 (100.0)

^a Ordered by latitude, North to South

^b Days with desert dust are defined as days with desert dust advection and estimated PM₁₀ concentrations at ground level > 0 µg/m³. Figures for days with and without desert dust do not add to the total number of days because of days with missing data on PM₁₀ concentrations at the rural monitoring site

^c Emilia Romagna includes the cities of Parma, Reggio Emilia, and Modena

Table 2. Estimated differences ($\Delta \pm \text{SE}$)^a between desert dust advection days and no-dust days^b in terms of daily mean PM₁₀ ($\mu\text{g}/\text{m}^3$), PM_{2.5} ($\mu\text{g}/\text{m}^3$), PM_{2.5-10} ($\mu\text{g}/\text{m}^3$), ozone ($\mu\text{g}/\text{m}^3$) and air temperature ($^{\circ}\text{C}$): city-specific and pooled results from a random-effects meta-analysis

City ^c	PM ₁₀	PM _{2.5}	PM _{2.5-10}	O ₃	Air temperature
Milan	10.0 \pm 2.0	6.1 \pm 1.7	2.7 \pm 0.8	-2.7 \pm 1.8	1.9 \pm 0.3
Turin	11.6 \pm 2.4	8.7 \pm 1.7	-	-0.6 \pm 1.9	1.4 \pm 0.2
Emilia-Romagna ^d	11.0 \pm 2.7	5.1 \pm 1.3	5.8 \pm 0.6	2.5 \pm 2.2	2.5 \pm 0.3
Bologna	12.3 \pm 1.4	7.3 \pm 1.2	-	-1.7 \pm 1.9	2.2 \pm 0.2
Marseille	9.4 \pm 0.8	4.6 \pm 1.0	2.7 \pm 0.7	11.4 \pm 1.6	2.2 \pm 0.2
Rome	8.8 \pm 0.8	2.8 \pm 0.6	5.9 \pm 0.4	-2.8 \pm 1.1	2.5 \pm 0.2
Barcelona	13.8 \pm 0.9	9.7 \pm 0.6	4.2 \pm 0.6	-1.7 \pm 1.1	2.1 \pm 0.2
Thessaloniki	10.0 \pm 1.8	6.6 \pm 1.1	3.9 \pm 0.9	-13.6 \pm 1.9	1.2 \pm 0.3
Madrid	21.2 \pm 1.0	9.8 \pm 0.7	11.6 \pm 0.8	-2.1 \pm 0.7	3.2 \pm 0.2
Palermo	16.7 \pm 0.9	-	-	-6.1 \pm 0.8	2.1 \pm 0.1
Athens	21.7 \pm 1.3	8.4 \pm 0.7	13.2 \pm 1.0	-2.2 \pm 1.0	2.3 \pm 0.2
POOLED	13.4 \pm 1.5	6.9 \pm 0.9	6.2 \pm 1.4	-1.8 \pm 1.8	2.2 \pm 0.2

^a Estimates are obtained from a multivariate linear regression model having dust advection indicator and dummies for months as predictors

^b Days with desert dust are defined as days with desert dust advection and estimated PM₁₀ concentrations at ground level $> 0 \mu\text{g}/\text{m}^3$

^c Ordered by latitude, North to South

^d Emilia Romagna includes the cities of Parma, Reggio Emilia, and Modena

Table 3. Estimated percent increase (95% CI) in risk of mortality and hospital admissions associated with 10 $\mu\text{g}/\text{m}^3$ increase in non-desert and desert PM_{10} ^a

Outcome	Lag	PM ₁₀			Non-desert PM ₁₀			Desert PM ₁₀		
		% IR (95% CI)	I ²	Het. p value	% IR (95% CI)	I ²	Het. p value	% IR (95% CI)	I ²	Het. p value
Mortality										
Natural	0-1	0.51 (0.27, 0.75)	22	0.23	0.55 (0.24, 0.87)	32	0.15	0.65 (0.24, 1.06)	0	0.75
Cardiovascular	0-5	0.66 (-0.02, 1.34)	40	0.08	0.49 (-0.31, 1.29)	46	0.04	1.10 (0.16, 2.06)	0	0.77
Respiratory	0-5	2.01 (0.92, 3.12)	31	0.15	2.46 (0.96, 3.98)	41	0.07	1.28 (-0.42, 3.01)	0	1.00
Hospital admissions										
Cardiovascular, age 15+	0-1	0.29 (0.00, 0.58)	41	0.10	0.37 (-0.04, 0.78)	59	0.02	0.32 (-0.24, 0.89)	0	0.50
Respiratory, age 15+	0-5	0.69 (0.20, 1.19)	32	0.17	0.62 (0.03, 1.21)	21	0.27	0.70 (-0.45, 1.87)	10	0.35
Respiratory, age 0-14	0-5	1.66 (0.93, 2.39)	0	0.47	1.82 (0.77, 2.88)	24	0.23	2.47 (0.22, 4.77)	9	0.36

I² statistics represents the amount (%) of heterogeneity among city-specific estimates; Heterogeneity p-value is calculated from the X² test on the Cochran's Q statistic

^a The estimates for non-desert and desert PM_{10} are obtained from two-pollutant models adjusted for the other PM source in turn, while the estimates for PM_{10} are from single-pollutant models

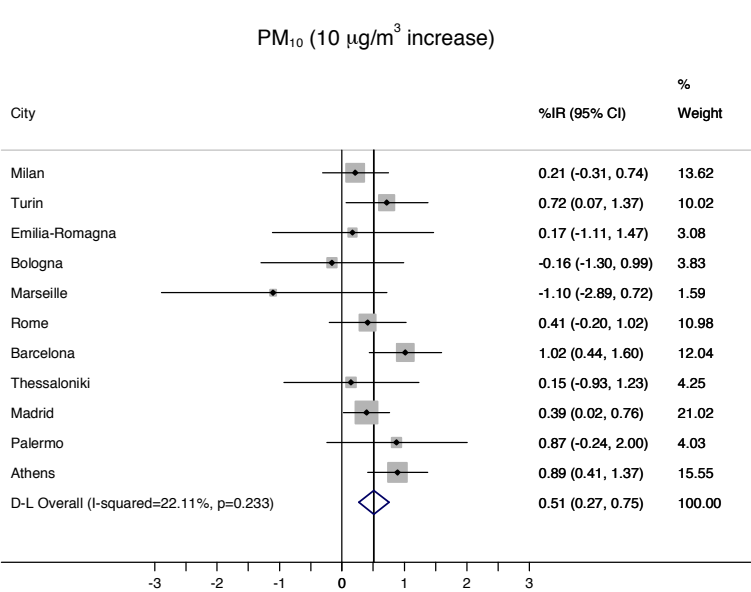
Figure Legends

Figure 1. Forest plot with results on estimated percent increases (95% CI) in risk of natural mortality associated with 10 $\mu\text{g}/\text{m}^3$ increase in total PM_{10} (A), non-desert PM_{10} (B) and desert PM_{10} (C). Points represents city-specific association estimates, with corresponding 95% confidence intervals (bars). The shaded boxes represent the weights attributed to each estimate in the meta-analysis. Finally, the diamond in the bottom part represents the meta-analytical effect estimate

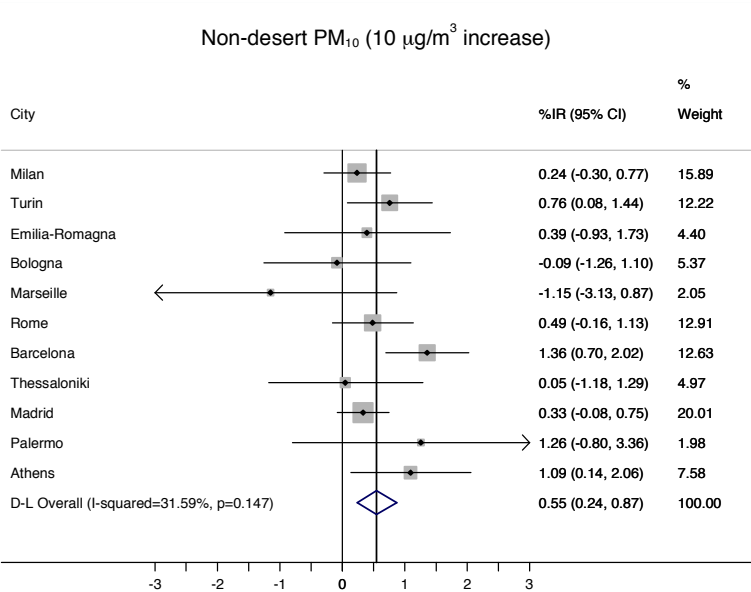
Figure 2. Estimated percent increase (95% CI) in risk of mortality (A) and hospital admissions (B) associated with 10 $\mu\text{g}/\text{m}^3$ increase in non-desert and desert PM_{10} , by season

Figure 1

(A)



(B)



(C)

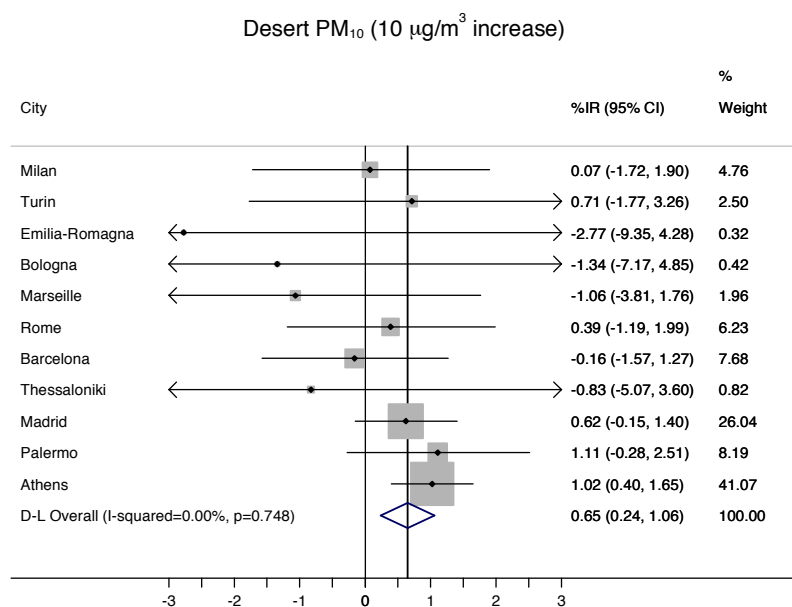
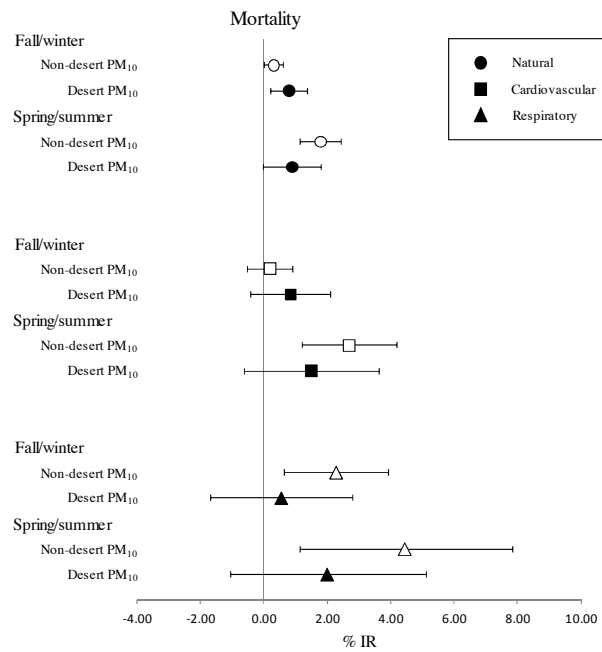


Figure 2

(A)



(B)

